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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,267	10/14/2003	Qingjie Ding	20861US4	4931

151 7590 11/16/2005  
HOFFMANN-LA ROCHE INC.  
PATENT LAW DEPARTMENT  
340 KINGSLAND STREET  
NUTLEY, NJ 07110

EXAMINER

PRYOR, ALTON NATHANIEL

ART UNIT PAPER NUMBER

1616

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/685,267	<b>Applicant(s)</b> DING ET AL.	
	<b>Examiner</b> Alton N. Pryor	<b>Art Unit</b> 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 26 August 2005.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 2 is/are allowed.
- 6) ☐ Claim(s) 1 and 3 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

**DETAILED ACTION**

Applicant's arguments filed 8/26/05 have been fully considered but they are not persuasive. See response below.

Examiner inadvertently made an error in the 103(a) rejection over Chong as being obvious over claims 1 and 3 on record. Examiner rejected claims 1 and 3 using the prior art (Chong) compound 1-(4-isothiocyanato-phenyl)-4-methyl-piperazine to make obvious the instant compound 4-(2-hydroxyethyl)-1-(4-isothiocyanatophenyl) piperazine; however, instant compound 1-(4-isothiocyanato-phenyl)-4-methyl-piperazine should have been rejected instead of instant compound 4-(2-hydroxyethyl)-1-(4-isothiocyanatophenyl) piperazine. This correction also sheds light on why claim 1 was included in the 103(a) rejection of record.

I. Rejection of claims 1 and 3 under 35 USC 103(a) as being obvious over Chong et al will be maintained for reason on record and reason as follows:

A. Applicant argues:

- 1) There is no motivation to modify Chong to obtain the compounds of the present invention.
- 2) The modification of Chong to arrive at the compounds of the instant invention would render the compounds of Chong unsatisfactory for their intended purpose. Chong teaches that the purpose of 1-methyl-4-nitrophenyl piperazine; 4-(4-methyl-piperazin-1-yl)-aniline; and 1-(4-isothiocyanato-phenyl)-4-methyl-piperazine are to act as compounds for use in the synthesis of {4-amino-2-[4-(4-methyl-

piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone. In contrast, compounds in the present invention have a methylethyl in place of the methyl in Chong's compounds.

- 3) By replacing Chong's intermediates with the methylethyl intermediates yields {4-amino-2-[4-(4-methylethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone instead of {4-amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone which are desired by Chong.
- 4) Chong discloses compounds as intermediates in the production of a final product; thus, one skilled in the art would not have been motivated to stop the reference synthesis and investigate the intermediate compounds.

Examiner argues:

- 1) There exist ample motivation to modify the compounds of Chong to obtain the compounds of the instant invention. Instant invention teaches homologs of the Chong's invention. Homologs are structurally similar compounds in terms of size, polarity, and electronegativity. Because of these factors, homologs would have similar physical and chemical properties and thus exhibit similar activity. Note, both Chong and instant inventor discloses that their compounds are used to treat cancer by inhibiting cyclin-dependent

kinases (CDK1, CDK2, etc.). For this reason it would have been obvious to modify the compounds of Chong to arrive at the compounds of the instant invention. See abstract and summary sections of both Chong and instant invention.

- 2) The modification of Chong to arrive at the compounds of the instant invention would render the compounds of Chong satisfactory for their intended purpose. Chong teaches that the purpose of 1-methyl-4-nitrophenyl piperazine; 4-(4-methyl-piperazin-1-yl)-aniline; and 1-(4-isothiocyanato-phenyl)-4-methyl-piperazine are to act as compounds for use in the synthesis of {4-amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone. The present invention discloses that the purpose of 1-methylethyl-4-nitrophenyl piperazine; 4-(4-methylethyl-piperazin-1-yl)-aniline; and 1-(4-isothiocyanato-phenyl)-4-methylethyl-piperazine are to act as compounds for use in the synthesis of {4-amino-2-[4-(4-methylethyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone. Note that the medicinal purpose of both Chong and instant invention is to treat cancer by inhibiting cyclin-dependent kinases (CDK1, CDK2, etc.). For this reason, the modification of Chong to arrive at the compounds of the instant invention would render the compounds of Chong satisfactory for their intended medicinal purpose.

Art Unit: 1616

- 3) Point 3 of Applicant arguments are addressed by a combination of points 1 and 2 of Examiner's response.
- 4) While it is true that 1-methyl-4-nitrophenyl piperazine; 4-(4-methyl-piperazin-1-yl)-aniline; and 1-(4-isothiocyanato-phenyl)-4-methyl-piperazine are intermediates in the synthesis of {4-amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone, it is also true that Chong discloses that these compounds, like methylethyl derivatives of the instant claims, are isolated and identified before the synthesizing {4-amino-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-thiazol-5-yl}-3,5-dichloro-pyridin-4-yl)-methanone. See Chong Example C(70) on pages 58-59. Note Example C(70): firstly, shows the synthesis, yield, and NMR of the nitro compound; secondly, shows treatment of the nitro compound with Pd-C to arrive at the amino compound (yield, NMR provided), and thirdly, employs the amino compound to arrive at the isothiocyanato compound (yield, NMR provided). Yields and NMR data supports that Chong's methyl compounds were synthesized, isolated, and identified.

***Allowable Subject Matter***

Claim 2 is allowable. The prior art does not teach or suggest the instant invention comprising 4-(2-hydroxyethyl)-1-(4-isothiocyanatophenyl)piperazine.

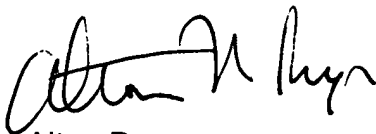
***Telephonic Inquiry***

Art Unit: 1616

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alton N. Pryor whose telephone number is 571-272-0621. The examiner can normally be reached on 8:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Alton N. Pryor', is written above the printed name.

Alton Pryor  
Primary Examiner  
AU 1616